Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 119-127 and 129-131 are pending in this application and are rejected on various grounds. The rejections to the presently pending claims are respectfully traversed.

Claim Rejections – 35 USC § 101 and 112, first paragraph

Claims 119-131 are rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility."

Claims 119-131 are further rejected under 35 U.S.C. §112, first paragraph allegedly "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention".

The Examiner alleges that "the asserted utilities of cancer diagnostics and cancer therapeutics for the claimed antibodies are credible and specific. However, they are not substantial. The data set forth...are preliminary at best". The Examiner maintains that further research would be required by the skilled artisan to determine if the disclosed results regarding a gene amplification event in tumors is also reflected at the mRNA and polypeptide levels and concludes that the asserted utility is not in currently available form, and the asserted utility is not substantial". For the reasons outlined below, Applicants respectfully disagree.

Utility Guidelines

In interpreting the utility requirement, in *Brenner v. Manson* [1] the Supreme Court held that the quid pro quo contemplated by the U.S. Constitution between the public interest and the interest of the inventors required that a patent applicant disclose a "substantial utility" for his or her invention, i.e. a utility "where specific benefit exists in currently available form." [2] The Court concluded that "a patent is not a hunting license. It is not a reward for the search, but

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[1] *Brenner v. Manson* 383 U.S. 519, 148 U.S.P.Q. (BNA) 689 (1966).

[2] *Id.* at 534, 148 U.S.P.Q. (BNA) at 695.

compensation for its successful conclusion. A patent system must be related to the world of commerce rather than the realm of philosophy." [3]

Later, in *Nelson v. Bowler* [4] the CCPA acknowledged that tests evidencing pharmacological activity of a compound may establish practical utility, even though they may not establish a specific therapeutic use. The court held that "since it is crucial to provide researchers with an incentive to disclose pharmaceutical activities in as many compounds as possible, we conclude adequate proof of any such activity constitutes a showing of practical utility." [5]

In *Cross v. Iizuka* [6] the CAFC reaffirmed *Nelson*, and added that *in vitro* results might be sufficient to support practical utility, explaining that "*in vitro* testing, in general, is relatively less complex, less time consuming, and less expensive than *in vivo* testing. Moreover, *in vitro* results with the particular pharmacological activity are generally predictive of *in vivo* test results, i.e. there is a reasonable correlation there between." [7] The court perceived "No insurmountable difficulty" in finding that, under appropriate circumstances, "in vitro testing, may establish a practical utility." [8]

The case law has also clearly established that applicants' statements of utility are usually sufficient, unless such statement of utility is unbelievable on its face. [9] The PTO has the initial burden that applicants' claims of usefulness are not believable on their face.[10] In general, an Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the

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[3] *Id.* at 536, 148 U.S.P.Q. (BNA) at 696.

[4] *Nelson v. Bowler*, 626 F. 2d 853, 206 U.S.P.Q. (BNA) 881 (C.C.P.A. 1980).

[5] *Id.* at 856, 206 U.S.P.Q. (BNA) at 883.

[6] *Cross v. Iizuka*, 753 F.2d 1047, 224 U.S.P.Q. (BNA) 739 (Fed. Cir. 1985).

[7] *Id.* at 1050, 224 U.S.P.Q. (BNA) at 747.

[8] *Id.*

[9] *In re Gazave*, 379 F.2d 973, 154 U.S.P.Q. (BNA) 92 (C.C.P.A. 1967).

[10] *Ibid*

utility requirement of 35 U.S.C. §101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." [11], [12]

Compliance with 35 U.S.C. §101 is a question of fact. [13] The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the totality of the evidence under consideration. [14] Thus, to overcome the presumption of truth that an assertion of utility by the applicant enjoys, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. **Absolute predictability is not a requirement.** Only after the Examiner made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence.

The well established case law is clearly reflected in the Utility Examination Guidelines ("Utility Guidelines") [15], which acknowledge that an invention complies with the utility requirement of 35 U.S.C. §101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility." Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that are to be diagnosed.

In explaining the "substantial utility" standard, M.P.E.P. §2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility

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[11] *In re* Langer, 503 F.2d 1380,1391, 183 U.S.P.Q. (BNA) 288, 297 (CCPA 1974).

[12] See, also *In re* Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *In re* Irons, 340 F.2d 974, 144 USPQ 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (CCPA 1977).

[13] *Raytheon v. Roper*, 724 F.2d 951, 956, 220 U.S.P.Q. (BNA) 592, 596 (Fed. Cir. 1983) cert. denied, 469 US 835 (1984).

[14] *In re* Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d (BNA) 1443, 1444 (Fed. Cir. 1992).

[15] 66 Fed. Reg. 1092 (2001).

requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "'substantial' utility."[16] Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement,[17] gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Proper Application of the Legal Standard

The Examiner maintains her previous conclusions that PRO1185 polypeptides lacks utility, that gene amplification does not necessarily result in increased expression at the mRNA and polypeptide levels and requotes Haynes *et al.*, Pennica *et al.* and Konopka *et al.* for support.

Applicants maintain that the specification provides sufficient disclosure to establish a specific, substantial and credible utility for native polypeptides with 80-99% identity to the PRO1185 polypeptide of SEQ ID NO:401 for the reasons outlined below. Applicants also maintain that a *prima facie* case has not been made for lack of utility by the Examiner and that the present disclosure is sufficient to establish a specific, substantial and credible utility for the PRO1185 polypeptide and other native polypeptides. Applicants address each rejection made by the Examiner below. In particular, it is maintained that the gene amplification assay discloses that the nucleic acid encoding PRO1185 is significantly overexpressed in human tumor tissues as compared to a non-cancerous human tissue control. Table 8 explicitly states that PRO1185 is significantly overexpressed in lung adenocarcinoma or colon tumors as compared to the normal control. The specification further teaches that these data demonstrate that the PRO1185 polypeptide of the present invention is also useful as a diagnostic marker for the presence of one or more lung adenocarcinoma or colon tumors in which it is significantly overexpressed.

Regarding Pennica *et al.*, Konopka *et al.* and Haynes, Applicants respectfully maintain that, for the reasons previously set forth in the Applicants' response filed July 16, 2004, these references do not show that a lack of correlation between gene (DNA) amplification and elevated

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16 M.P.E.P. §2107.01

17 M.P.E.P. §2107 II (B) (1)

mRNA levels, in general, exists. For example, Pennica discusses WISP genes only, and not genes in general, and therefore it does not teach that *it is more likely than not* that gene amplification is not associated with increased mRNA or increased protein levels. Similarly, Konopka only addresses the *abl* gene, again not genes in general, and is therefore not an appropriate reference for making a *prima facie* case for lack of utility. In fact Haynes, contrary to the Examiner's reading, teaches that "there was a ***general trend but no strong correlation*** between protein [expression] and transcript levels" (Emphasis added). For example, in Figure 1, Haynes shows a positive correlation between mRNA and protein levels amongst most of the 80 yeast proteins studied. Moreover, very few data points deviated or scattered away from the expected normal and no data points showed a negative correlation between mRNA and protein levels for the 80 yeast proteins. Haynes discloses that protein levels could not be accurately predicted. As discussed above, the law does not require the existence of a "strong" or "linear" correlation between mRNA and protein levels. Nor does the law require that protein levels be "accurately" predicted from the mRNA data. As long as there is a general trend amongst the proteins studied, this reference meets the "more likely than not standard." Indeed, according to the authors themselves, the data showed a general trend between protein expression and transcript levels, which meets the "more likely than not standard" and shows a positive correlation between mRNA and protein. Therefore, Applicants submit that the Examiner's reasoning is based on a misrepresentation of the scientific data presented in Haynes *et al*, and application of an improper, heightened legal standard.

The Examiner says on page 5 of the Office action that "(n)o evidence has been submitted that it is the norm rather than the exception that protein levels are increased when gene amplification occurs in cancer." Applicants respectfully disagree. Applicants presented three articles Orntoft, Hyman and Pollack *et al.* previously and the data presented in these papers clearly showed that a large number of genes which were amplified in tumor cells showed increased gene expression and due to this showing in a large number of genes, the teachings met the "*more likely than not*" standard. Therefore, contrary to what the Examiner contends, the art clearly indicates that if a gene is amplified in cancer, it is more likely than not that the encoded protein will also be expressed at an elevated level.

In conclusion, applicants maintain that the Examiner has not shown that a lack of correlation exists between gene amplification and polypeptide over-expression based on the

teachings of Pennica, Konopka and Haynes, as discussed above. In fact, contrary to what the Examiner contends, the art indicates that, if a gene is amplified in cancer, it is **more likely than not** that the encoded protein will be expressed at an elevated level. Thus, Applicants have demonstrated a credible, specific and substantial asserted utility for the PRO1185 polypeptide based on the gene amplification results for the nucleic acid, for example, in detecting over-expression or absence of expression of PRO1185. Based on these teachings, one skilled in the art would know how to use the claimed polypeptides without undue experimentation at the time the application was filed.

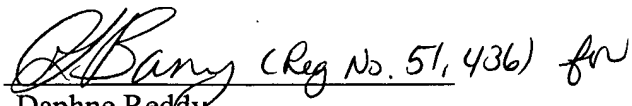
Thus, Applicants have demonstrated utility for the PRO1185 polypeptide as a marker for adenocarcinomas of the lung or colon. Accordingly, the present 35 U.S.C. §101 and §112, first paragraph utility rejections should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C42). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,s

Date: May 23, 2005



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